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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/726,029	12/02/2003	Joan D. Leonard	12780/102	4719

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 09/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/726,029	LEONARD ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *2 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.0.05

DETAILED ACTION

Claim Objection

1. Claim 29 is objected to for the following informality: Claim 29 should end with a period(.). Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 21-57 are rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 39 in particular, recite the phrase " ...derived from...". It is unclear as to what the applicant is referring? Thus, the metes and bounds of the phrase cannot be ascertained. Clarification is required.

3. Claims 21-57 are rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 47 in particular, recites method steps such as isolating, amplifying, separating and comparing different *M. bovis* biotypes. It is unclear as to what the applicant is referring since the claims are directed to a method of immunizing bovine. The method steps of claim 47 appear to be directed to a method of preparing and comparing different *M. bovis* biotypes and not a method of immunizing bovine. A method of preparing and comparing different *M. bovis* biotypes is different from the

claimed method of immunizing bovine. All claim limitations should be directed to a method of immunizing bovine since that is the invention under examination. Correction is required.

4. Claims 53- 57 are rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It appears that the outcome of the method is different from the preamble. The claims are drawn to a method of immunizing. The result of the immunizing should be to protect against infection, but the result is reducing the incidence of mastitis. It would appear that the claims should be drawn to method of reducing mastitis. However, a method of immunizing is current being examined and not a method of reducing mastitis. Therefore, all claim limitations as well as the result of the claim limitations should be directed to a method of immunizing bovine. Correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 21-30, 50 and 52 are rejected under 35 U.S.C. 102(b) as anticipated by Boothby et al *(Cornell Vet. 1986, April, 76(2), 188-197).*

Claims 21-30, 50 and 52 are drawn to a method of immunizing bovine animals comprising administering to bovine animals at least one inactivated or attenuated *Mycoplasma bovis*, whereby the incidence of mastitis in the bovine animals is reduced.

Boothby et al teach a method of immunizing bovine by subcutaneously administering to bovine formalin killed *M. bovis* in Freund's complete adjuvant (page 190). Boothby et al teach that a composition comprising formalin inactivated *M. bovis* protein was infused into the quarters of cows (page 190). Therefore, the prior art teaches the claim limitation "...administering to bovine animals an antigenic component from at least on inactivated or attenuated *M. bovis* biotype. Boothby et al teach that it is apparent that vaccination resulted in a reduced duration of infection (page 194). Therefore, the prior art teaches the claim limitations"...where the administering results in less clinical disease in the bovine animal" and "...whereby the incidence of mastitis in bovine animals is reduced". Claim limitations such as "... comprising administering at least one inactivated *M. bovis* to about 50% of the herd " is viewed as optimizing experimental parameters.

Since the Office does not have the facilities for examining and comparing applicant's method with the method of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of the prior art (i.e., that the method of the prior art does not possess the same material

method steps and parameters of the claimed method). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 21-31, 50 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boothby et al *(Cornell Vet. 1986, April, 76(2), 188-197)* and in view of Koshi et al, *(Journal of Biological Standardization 1976, 4, 151-154).*

Claims 21-31, 50 and 52 are drawn to a method of immunizing bovine animals comprising administering to bovine animals at least one inactivated or attenuated *Mycoplasma bovis*, whereby the incidence of mastitis in the bovine animals is reduced, wherein the *Mycoplasma bovis* has been inactivated by treatment with β-propiolactone.

Boothby et al teach a method of immunizing bovine by subcutaneously administering to bovine formalin killed *M. bovis* in Freund's complete adjuvant (page 190). Boothby et al teach that a composition comprising formalin inactivated *M. bovis* protein was infused into the quarters of cows (page 190). Therefore, the prior art teaches the claim limitation "...administering to bovine animals an antigenic component from at least on inactivated or attenuated *M. bovis* biotype. Boothby et al teach that it

is apparent that vaccination resulted in a reduced duration of infection (page 194). Therefore, the prior art teaches the claim limitations"...where the administering results in less clinical disease in the bovine animal" and "...whereby the incidence of mastitis in bovine animals is reduced". Claim limitations such as "... comprising administering at least one inactivated *M. bovis* to about 50% of the herd " is viewed as optimizing experimental parameters.

Boothby et al does not teach β-propiolactone inactivation.

Koshi et al teach that mycoplasmas can be successfully inactivated by β-propiolactone (page 153). Koshi et al teach that data provided in this study can provide a reference point for inactivation of mycoplasmas using β-propiolactone, formalin or phenol (page 154).

It would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use β-propiolactone to inactive *Mycoplasma bovis* used in the method of immunizing bovine as taught by Boothby et al because Koshi et al demonstrates that mycoplasmas can be inactivated used as little as 0.05% of β-propiolactone in 2 hours (page 153). It would be expected barring evidence to the contrary that β-propiolactone would be effective in inactivating mycoplasmas.

7. Claims 21-38, 42, 50 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boothby et al and Koshi et al as applied to claims 21-31, 50 and 52 and in further view of Poumarat et al *(Veterinary Microbiology, Volume 40, 1994, p. 305-321).*

Claims 21-38, 42, 50 and 52 are drawn to a method of immunizing bovine animals comprising administering to bovine animals at least two inactivated or attenuated *Mycoplasma bovis*, whereby the incidence of mastitis in the bovine animals is reduced.

The teachings of Boothby et al and Koshi et al have been described above.

Boothby et al and Koshi et al do not teach different *M. bovis* biotypes.

Poumarat et al teach different M. bovis biotypes. Poumarat et al disclose Restriction endonuclease analysis (REA) with three enzymes *Sma*I, *Pst*I, and *Bam*I which were used to identify 13 different genomic groups (i.e. biotypes) among 37 *Mycoplasma bovis* strains (see the Abstract). Poumarat et al disclose 37 bovis strains studied gave five different electrophoretic patterns with BamHI, four with *Sam*I and five with *Pst*I (figure 1). Poumarat et al further disclose that based on the combination of the different electrophoretic profiles obtained with the three enzymes, the 37 strains could be classified in 13 genomic groups (table 2).

It would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add the *Mycoplasma bovis* isolates of Poumarat et al to the vaccine composition as taught by Boothby et al and Koshi et al used in the method of immunizing bovine as combined above because Poumarat et al teach that there is a marked intraspecies genomic heterogeneity among isolates of *Mycoplasma bovis* collected from different geographic origins and that antigenic variability must be taken into account in developing diagnostic and vaccination strategies (page 319).

8. Claims 21-38, 42-45 and 47-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boothby et al, Koshi et al, Poumarat et al as applied to claims 21-38, 42, 50 and 52 and further view of Rawadi *(G.A., Characterization of Mycoplasmas by RAPD Fingerprinting, Methods in Molecular Biology, 104:179-187).*

The teachings of Boothby et al, Koshi et al and Poumarat et al have been described above.

Boothby et al, Koshi et al and Poumarat et al do not teach using DNA polymorphisms to determine different *M. bovis* biotypes.

Rawadi teaches that Mycoplasmas can be characterized by random amplification polymorphic DNA (RAPD) (page 179). Rawadi teaches that RAPD generates a genomic fingerprint that can be used as a "personal signature" of a particular species (page 180).

It would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to test for different biotypes of *Mycoplasma bovis* used in the method of immunizing bovine as combined above by using DNA polymorphisms because Rawadi teaches that RAPD generates a genomic fingerprint that can be used as a "personal signature" of a particular species (page 180). It would be expected barring evidence to the contrary that RAPD can be used to distinguish between biotypes within a species because Rawadi teaches that difference in DNA fingerprints between two cells can be detected and is a sign of polymorphism during the evolutionary process or mutations that may have occurred throughout the generation (page 180).

9. Claims 21-39, 41-45 and 47-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boothby et al, Koshi et al Poumarat et al, Rawadi as applied to claims 21-38, 42-45 and 47-57 and in further view of Norcross et al (*U.S. Patent No: 4,425,330 published January 10, 1994).*

The teachings of Boothby et al, Koshi et al Poumarat et al and Rawadi have been described above.

Boothby et al, Koshi et al Poumarat et al and Rawadi do not teach an antigen derived from another pathogen.

Norcross et al teach a method of preventing and controlling gram-positive cocci such as *Staphylococcus aureus* induced bovine mastitis infections by administering to bovine a vaccine comprising *S. aureus* and *Streptococcus agalactiae* antigens (see the Abstract).

It would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add killed antigens from other pathogens such as *Staphylococcus aureus* to the vaccine compositions used in the method of immunizing bovine as combined above because Norcross et al teach that demonstrates that vaccine compositions comprising *S. aureus* and *S. agalactiae* can prevent or control mastitis in bovine (see the Abstract) and Boothby et al teach administering vaccine compositions comprising formalin killed *M. bovis* reduces duration of *M. bovis* infections(page 194). It would be expected that a vaccine composition comprising inactivated *M. bovis* strains of multiple biotypes, *S. aureus* and *S. agalactiae*, a pharmaceutically acceptable excipient and a suitable adjuvant would be effect against

bovine mastitis in cattle because Norcross et al teach that the preferred vaccine for broad applicability are adapted for a specific locale where the causative agent or agents have been isolated and the vaccine is tailored to combat manifestations of disease for that particular area (column 7). Therefore, a preferred vaccine composition would comprise "in total combination" antigens to prevent or control bovine mastitis.

10. Claims 21- 45 and 47-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boothby et al, Koshi et al Poumarat et al, Rawadi as applied to claims 21-39, 41-45 and 47-57 and in further view of Straub *(Comp Immunol Microbiol Infect Dis., 1991; 14(2):175-86).*

The teachings of Boothby et al, Koshi et al Poumarat et al and Rawadi have been described above.

Boothby et al, Koshi et al Poumarat et al and Rawadi do not teach attenuated or inactivated viruses.

Straub teaches that bovine herpesvirus type 1 (BHV1) causes a catarrhal type of mastitis (page 177). Straub teaches that a number of monovalent and multivalent BHV1 vaccines (comprises BHV1, bovine respiratory syncytial virus (BRSV) and parainfluenza type 3 (PI3)) are licensed throughout the world (page 182). Straub teaches that both attenuated and inactivated BHV1 vaccines protect against BHV1 infections (page 182).

It would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add bovine viruses from other pathogens such as bovine herpesvirus type 1, bovine respiratory syncytial virus and parainfluenza type 3 to the

vaccine compositions as taught by Straub used in the method of immunizing bovine as combined above because can prevent bovine infectious disease, including mastitis (page 183) and Boothby et al teach administering vaccine compositions comprising formalin killed *M. bovis* reduces duration of *M. bovis* infections (page 194). It would be expected that a vaccine composition comprising inactivated *M. bovis* strains of multiple biotypes, bovine viruses such as BHV1, BRSV and PI3, a pharmaceutically acceptable excipient and a suitable adjuvant would be effective in a method of immunizing against bovine mastitis in cattle because Boothby et al have demonstrated that *M. bovis* protect against mastitis in bovine and Straub has demonstrated that bovine herpesvirus type 1 protects against bovine infectious disease, including mastitis. Additionally, Straub teaches that BVH1 infections are frequently complicated by bacterial infections as well as occurring simultaneously with bovine virus diarrhea and/or parainfluenza type 3 (see the Abstract). Therefore, one of ordinary skill in the art would reasonably conclude that a multivalent vaccine comprising viruses as well as bacteria would be effective in immunizing bovine against mastitis.

Status of Claims

11. No claims are allowed.

12. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

VLF

Vanessa L. Ford
Biotechnology Patent Examiner
May 24, 2005

LRS

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